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DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the food constituent, the constituent for the oral cavities, and physic constituent for gum disease prevention or a therapy.

[0002]

[Description of the Prior Art] A matrix METARO protease (it abbreviates to MMPs a Japanese name 'a matrix metalloprotein dialytic ferment' and henceforth) is the generic name of the extra-cellular-matrix dialytic ferment characterized by holding zinc (II) ion in an active site. The metabolic turnover of this extra-cellular matrix is mainly adjusted by the balance of MMPs and organization origin METARO protease inhibitor (TIMP) specific to MMPs. It is known that collapse of the abnormalities in structure of an extra-cellular-matrix component based on the abnormalities in a manifestation of MMPs and the metabolic turnover balance of composition and decomposition is connected with gum disease, such as periodontitis.

[0003] As MMPs, ten or more kinds of enzyme molecular species, such as collagenase (MMP- 1 and 8), SUTOROME lysin (MMP-3), and gelatinase (MMP- 2 and 9), are known (185 Yoshiwara, a new name: inflammation, immunity, 2,177- 1994), and these are produced by the cell of many kinds.

[0004] Also in gum disease, such as gingivitis and periodontitis, it is thought that MMPs is participating in the onset and advance of gum disease deeply, and it is suggested that MMPs which participates in the organization destruction in gum disease, such as gingivitis and periodontitis, is the collagenase and gelatinase which a Homo sapiens gingival-epithelium cell, gum fibroblast, and a periodontium cell mainly produce. Namely, gum disease, such as gingivitis and periodontitis, happens, when a specific gum disease original bacillus (P. gingivalis bacillus) infects the periodontium. The epithelial cell and gum fibroblast in the periodontium which received the outpatient department stimulus by the disease germ, As a result of producing MMPs from a periodontium cell, when the periodontium structure where a gear tooth and the periodontium are combined is destroyed by the cell origin MMPs, symptoms mainly develop. It is thought that it goes on (926 M. Kylmaniemi et al:J.Dent Res., 75:919- 1996). Moreover, the activity of the periodontium origin MMPs increasing easily also according to a factor which changes the immune response nature of living bodies, such as individual smoking habit and a diabetes-mellitus disease, and increasing the onset and the percentage of completion of gum disease, such as gingivitis and periodontitis, is suggested.

[0005] Therefore, the tetracycline it is reported that it is it being thought that the inhibitor of MMPs is promising for the therapy or prevention of periodontitis, gingivitis, etc. of gum disease, for example, checking MMPs of gum fibroblast and the epithelial cell origin in periodontitis, and its qualification object (385 L. H.Nip et al:J.Periodont Res., 28:379- 1993) are actually applied as a therapy adjuvant of periodontitis.

[0006] However, if the appearance risk of the resistant bacteria in the side effect and the inside of the body peculiar to a tetracycline antibiotic which are synthetic material is taken into consideration, it is not desirable to take in these antibiotics for a long period of time in order to treat or prevent gum disease,

such as periodontitis. Therefore, a MMP inhibitor which is the natural product origin with few side effects by recipe and intake, and has inhibitory action to MMPs of the periodontium origin is desired. And sufficient MMPs inhibition effectiveness needs to be demonstrated with the suitable intake usually considered.

[0007] Here, as a MMPs inhibitor of the natural origin, it is reported, for example that the flavones or anthocyanidins of the natural product origin has MMPs inhibitory action (JP,08-104628,A). as the inhibitor of the natural origin to the collagenase which is one sort of MMPs -- *Schizonepeta tenuifolia* extractives or peppermint extractives (JP,06-183990,A), and a NORUJIHIDOROGUAYARE tech -- acid (JP,04-217626,A) and PORIPORE nick acid C (JP,09-40552,A) are reported. moreover, the 4 ring type by which separation purification was carried out from the HOUFUKU low bamboo -- triterpene 20-carboxy-16-hydroxy-21-nor-5 It is also reported that alpha-7, 9(11)-lanostadien-3, and 24-dione have collagenase inhibitory action (JP,9-235293,A).

[0008] It is reported that the catechins contained in tea show a procaryote cell and the inhibitory action to the collagenase of the eukaryote cell origin, and the inhibitory action to the collagenase of a gum disease patient's gingival-sulcus decoction origin is shown (636 M.Makimura et al:J.Periodontol., 64 (7):630- 1993).

[0009] Moreover, as for green tea extract polyphenol, the caries, the preventive effect (JP,04-27204,B) of gum disease, etc. are reported.

[0010] The supply food (trade name Body Language, Oxyfresh, and U.S.) which blended coenzyme Q 10 with the BUTOU seed extractives with which it is reported that the inhibition effectiveness is shown to the collagenase of a part of bacillus origins (L. 38:608 Robert et al:Path.Biol and 1990) and which solicits gum anti-inflammations is sold in the U.S.

[0011] On the other hand, in the combination of the hydrophilic polyphenol (for example, pro anthocyanidin) which has the structure of the catechin or the flavonolignan, and oleophilic carotenoid or oleophilic pro carotenoid (for example, vitamin E), the synergistic effect of both antioxidation activity is reported from a viewpoint of an antioxidation operation (JP,07-196534,A).

[0012]

[Problem(s) to be Solved by the Invention] The purpose of this invention is to offer the constituent with high safety which was excellent in prevention or the curative effect of gum disease, and was excellent in prevention or a curative effect to the gum disease from which especially smoking causes exacerbation especially a food constituent, the constituent for the oral cavities, and a physic constituent.

[0013]

[Means for Solving the Problem] By using the extract containing natural polyphenol combining one or more sorts of vitamin C (and the salt), vitamin E, vitamin A, and B-carotene, as a result of inquiring wholeheartedly, this invention person found out that the inhibition effectiveness of MMPs was reinforced, found out that the gum disease prevention thru/or the curative effect which was excellent with the constituent containing these was acquired, and completed this invention.

[0014] Moreover, it found out that the effectiveness which it is ineffective to it being possible to remove the stimulation to the periodontium of a gum disease original bacillus by considering as the constituent containing the plant extract which has antimicrobial activity further, and prevents or treats gum disease about the combination of the extract containing natural polyphenol and the above-mentioned vitamins was reinforced.

[0015] Furthermore, when this invention person used together the extract which contains natural polyphenol under a nicotine environment, and the above-mentioned vitamins, he found out that the effectiveness which controls MMPs concentration increase became strong further. Here, nicotine is the main stimulator in cigarette smoke, and doing bad influences, such as growth control of a cell and increase of collagenase production, to a periodontium cell by stimulus of nicotine is reported by the in vitro trial. Therefore, smoking is attracted, an smoker tends to show the symptoms of gum disease, and advance is also early. Moreover, if it is under a nicotine environment even if it is a passive smoker, like an smoker, it is easy to show the symptoms of gum disease, and is in the inclination for advance to be early. As mentioned above, this invention person found out controlling effectively increase of the MMPs

concentration in the oral cavity from which smoking becomes a cause with the extract containing natural polyphenol, and the constituent containing the above-mentioned vitamins.

[0016] That is, this invention is a term 1. (A) One sort or two sorts or more which are chosen from the extract containing natural polyphenol, To a list, it is (B). One sort or two sorts or more which are chosen from the group which becomes vitamin C and its salt, vitamin E, and a vitamin A list from B-carotene, The gum disease prevention to contain or the food constituent for a therapy, term 2 (A) The extract containing natural polyphenol A constituent given in the term 1 which is one sort chosen from the group which consists of grape seed extractives, a tea extract, blueberry extractives, and Silymarin extractives, or two sorts or more, Term 3 It is (C) further. The term 1 containing antibacterial vegetable extractives, or a constituent given in 2, Term 4 (C) A constituent given in the term 3 which is one sort chosen from the group which antibacterial vegetable extractives become from an oil solubility glycyrrhiza extract and mulberry bark extractives, or two sorts, Term 5 Have the depressant action of the periodontium cell origin matrix METARO protease production by nicotine stimulus. A constituent given in either of the terms 1-4 especially useful to an smoker, term 6 One sort or two sorts or more which are chosen from the extract containing (A) natural polyphenol, To a list, it is (B). One sort or two sorts or more which are chosen from the group which becomes vitamin C and its salt, vitamin E, and a vitamin A list from B-carotene, The gum disease prevention to contain or the constituent for the oral cavities for a therapy, term 7 (A) One sort or two sorts or more which are chosen from the extract containing natural polyphenol, To a list, it is (B). The physic constituent for gum disease prevention or a therapy containing one sort chosen from the group which becomes vitamin C and its salt, vitamin E, and a vitamin A list from B-carotene, or two sorts or more is started.

[0017] The physic constituent for the constituent for the oral cavities for gum disease prevention of this invention or the food constituent for a therapy, gum disease prevention, or a therapy and gum disease prevention, or a therapy may only be called "this invention constituent."

[0018] In addition, in this invention constituent, prevention of gum disease means preventing the onset of gum disease, and delaying advance of gum disease.

[0019] moreover, this invention -- setting -- "an smoker" -- an smoker -- a passive smoker besides him also contains.

[0020]

[Embodiment of the Invention] Below, this invention is explained at a detail.

[0021] Although especially limitation is not carried out if the expected effectiveness of this invention is shown when it combines with the vitamins used by this invention as an extract containing the natural polyphenol used for this invention constituent, the extract which contains the natural polyphenol which has a flavonoid frame, a catechol, phloroglucine, etc., for example is mentioned. Moreover, the extract which contains the natural polyphenol which has MMPs inhibition activity especially as natural polyphenol is desirable.

[0022] The periosteum [in / for example / as natural polyphenol / rheumatoid arthritis and the osteoarthritis] and articular cartilage organization; cornea tissue; periodontium which have MMPs inhibition activity; what has inhibition activity to the cell origins MMPs, such as a cancer organization, in a list is mentioned. Especially the natural polyphenol that has inhibition activity to the periodontium cell origin MMPs also in them is desirable.

[0023] As natural polyphenol which has inhibition activity to such the periodontium cell origin MMPs, the natural polyphenol which has a flavonoid frame is mentioned, for example.

[0024] Specifically as natural polyphenol which has the above-mentioned flavonoid frame, catechins; anthocyanidins, such as pro anthocyanidin; epigallocatechin, epicatechin, and GAROKATEKIN, and anthocyanins can be illustrated.

[0025] As an extract (it considers as a "natural polyphenol extract" hereafter) containing the natural polyphenol used for this invention constituent, it is desirable to use natural polyphenol extracts, such as grape seed extractives obtained from a grape seed, for example, a tea extract obtained from tea, blueberry extractives obtained from a blueberry, and the Silymarin extractives obtained from a thistle, and it is desirable to use especially grape seed extractives.

[0026] In this invention, a natural polyphenol extract may be used independently and may be used combining two or more sorts. When using combining two or more sorts, it is desirable to use grape seed extractives combining other natural polyphenol extracts, the combination of grape seed extractives, a tea extract and grape seed extractives, blueberry extractives and grape seed extractives, and the Silymarin extractives is desirable especially, and the combination of grape seed extractives and a tea extract is desirable also especially in these combination.

[0027] Although it is not limited as loadings of the natural polyphenol extract in this invention constituent especially as long as gum disease can be prevented thru/or treated, it is desirable to blend 0.001 to 40% of the weight especially 0.0005 to 75% of the weight as extract dry weight as opposed to the total weight of a constituent. When making this invention constituent into a food constituent especially, and ****ing to the constituent for the oral cavities 0.01 to 20% of the weight, it is desirable to blend 0.01 to 1% of the weight.

[0028] If the expected effectiveness of this invention can be acquired, what was obtained using the approach used commonly can be used for the natural polyphenol extract used in this invention, without limiting especially.

[0029] as an extracting solvent which extracts a natural polyphenol extract, alcohols; ethyl-acetate ester, such as a water; methanol, ethanol, propanol, and a butanol, etc. is low-grade, for example -- hydrocarbons [, such as alkyl ester; benzene and a hexane,]; -- in addition to this, well-known solvents, such as ethyl ether, an acetone, and an acetic acid, can be mentioned. These solvents may be used independently and can also be used combining two or more sorts.

[0030] As extract operation, a well-known approach which is usually used is employable.

[0031] In this invention, although the extract obtained by the above approaches used commonly may be used as it is, what was condensed further may be used for it if needed. Moreover, it is also possible to refine and use an extract using the purification method used commonly, for example, a countercurrent distribution method, liquid chromatography, etc.

[0032] In this invention, a natural polyphenol extract can also be used as a dry matter. As an approach of manufacturing the dry matter containing natural polyphenol, although especially limitation is not carried out, the approach of using as a vegetable extractives dry matter the vegetable extract obtained as mentioned above, for example with the usual means, such as reduced pressure drying and freeze drying, is mentioned.

[0033] The grape seed extractives which can be used as a natural polyphenol extract in this invention It is what is obtained considering the seed of the Europe grape (*Vitis vinifera*) as a raw material. As polyphenol The grape seed extractives used for this invention which is a thing containing the pro anthocyanidin and anthocyanins which have MMPs inhibition activity, and which are polyphenol For example, it may be obtained by the above well-known approaches, and JP,06-31208,B, JP,63-162685,A, JP,03-200781,A, JP,02-48593,A, publication number It may be obtained by the approach indicated by official reports, such as No. 99090 [03 to].

[0034] In addition, as a food material, grape seed extractives which were indicated by these official reports are sold from KIKKOMAN CORP. (trade name; KPA, Gravinol) and an in dinner company (trade name; leuco selection), and can come to hand.

[0035] Although the loadings in the case of blending grape seed extractives in this invention constituent are not limited especially if desired effectiveness is acquired, it is desirable to blend ten to 50% of the weight especially 0.005 to 75% of the weight as extract dry weight to this invention constituent whole quantity. Moreover, although especially the loadings are not limited when using grape seed extractives together with other natural polyphenol extracts of this invention, it is desirable to blend grape seed extractives in the above-mentioned amount, and to blend other natural polyphenol extracts ten to 50% of the weight especially 0.005 to 75% of the weight as extract dry weight to this invention constituent whole quantity. Moreover, when using together grape seed extractives and other natural polyphenol extracts, and this invention constituent is a food constituent, and it is 0.01 - 40 % of the weight, and a constituent for the oral cavities about other natural polyphenol extracts, it is desirable to blend other natural polyphenol extracts 0.01 to 5% of the weight.

[0036] Especially when blending grape seed extractives with this invention constituent and considering as a solid gestalt thru/or solid pharmaceutical forms, such as troches, a tablet, a capsule, a candy, and chewing gum, it is desirable as extract dry weight to blend 1.0 to 10% of the weight 0.5 to 20% of the weight. Moreover, when making this invention constituent which blended grape seed extractives into the gestalt thru/or pharmaceutical forms of a liquid, such as juice, it is desirable to blend 0.005 to 0.5% of the weight as extract dry weight.

[0037] In this invention, the tea extract is selectable considering green tea including the tea (*Camellia sinensis*) generally drunk, oolong tea, tea, PUARU tea, etc. as a raw material. As for a tea extract, it is desirable to use the tea extract which contains the polyphenol of catechins, such as epigallocatechin which has MMPs inhibition activity, epicatechins, and GAROKATEKIN, as natural polyphenol, and contains these polyphenol 65% or more 30% or more especially in this invention. When using a tea extract in this invention, what is obtained by the above well-known approaches may be used, and what was obtained by the approach indicated by JP,64-90124,A and JP,1-265023,A may be used.

[0038] In addition, a tea extract is sold from Mitsui agriculture-and-forestry incorporated company (trade name; polyphenon) and TAIYO KAGAKU CO., LTD. (trade name; Sunphenon), and is available.

[0039] Although the loadings in the case of using a tea extract in this invention constituent are not especially limited if desired effectiveness is acquired, it is desirable to blend ten to 50% of the weight especially 0.005 to 75% of the weight as extract dry weight to this invention constituent whole quantity for example. Especially when considering as a solid gestalt thru/or solid pharmaceutical forms, such as troches, a tablet, a capsule, a candy, and chewing gum, especially, it is desirable to blend 1.0 to 10% of the weight 0.5 to 20% of the weight.

[0040] Blueberry extractives are obtained considering various kinds of blueberries as a raw material, and contain the anthocyanidins which are polyphenol which has MMPs inhibition activity as polyphenol. What extracted by approach which was described above, and which is used commonly also when using blueberry extractives in this invention can be used. Moreover, the dry matter of alcoholic-drainage system extract of blueberry extractives is sold from the in dinner company, for example, and it is also possible in this invention to use the dry matter concerned.

[0041] Also when using the Silymarin extractives in this invention, what was extracted by the above approaches used commonly can be used. Furthermore, since the Silymarin extractives are sold from Api Co., Ltd. and can come to hand, the Silymarin extractives concerned may be used for them by this invention.

[0042] the extract which contains natural polyphenol in this invention constituent -- in addition, it is also possible to contain the natural polyphenol which has the MMPs inhibition activity in an extract which was described above combining one sort chosen from the group which becomes the following vitamin C and its salt, vitamin E, and a vitamin A list from B-carotene, or two sorts or more.

[0043] as the natural polyphenol which is the active principle which has the MMPs inhibition activity in an extract -- the above -- pro -- catechins; anthocyanidins, such as anthocyanidin; epigallocatechin, epicatechin, and GAROKATEKIN, and anthocyanins may be mentioned, and these are independent, or they may be combined two or more sorts and may be used.

[0044] Moreover, it is also possible to consider as the food constituent, the constituent for the oral cavities, and physic constituent the gum disease prevention which contains one sort of the natural polyphenol which has the MMPs inhibition activity in an extract which was described above instead of the extract containing natural polyphenol, or two sorts or more combining one sort chosen from the group which becomes the following vitamin C and its salt, vitamin E, and a vitamin A list from B-carotene, or two sorts or more, or for a therapy.

[0045] About the method of preparation of the gestalt of the class of component of the class of vitamins, such as loadings of the natural polyphenol concerned in the constituent which blends the natural polyphenol which replaces with the extract containing natural polyphenol and has MMPs inhibition activity, and vitamin C, or loadings, and others or loadings, and a constituent or a pharmaceutical form, and a constituent, it is the same as that of the constituent which uses a natural polyphenol extract

combining this invention vitamins.

[0046] In this invention constituent, it is vitamin C (L-ascorbic acid: VC) and its salt, vitamin E (alpha-tocopherol: VE), vitamin A, and the B-carotene that are used combining a natural polyphenol extract (it may be hereafter called the "this invention vitamins"). As a salt of vitamin C (L-ascorbic acid), sodium salt, a calcium salt, the salt of the first iron, the salt of palmitic-acid ester, etc. are mentioned. These this invention vitamins may be used independently, and two or more sorts may be chosen and used for it.

[0047] As combination in the case of choosing two or more sorts, this invention vitamin It reaches vitamin C (or the salt). Vitamin-E; vitamin C (or the salt), vitamin A; vitamin C (or the salt), B-carotene; vitamin E, vitamin A; vitamin E, B-carotene; vitamin A, and B-carotene; vitamin C (or the salt), Vitamin E and vitamin A; Vitamin C (or the salt), vitamin E, and B-carotene; vitamin C (or the salt), Vitamin A and B-carotene; the combination of vitamin E, vitamin A and B-carotene; vitamin C (or the salt), vitamin E, vitamin A, and B-carotene is mentioned.

[0048] It is desirable to blend 0.0005 - 50 % of the weight with them as this invention vitamin whole quantity to this invention constituent whole quantity, although the loadings of B-carotene are not limited to the vitamin C in this invention constituent and its salt, vitamin E, and a vitamin A list especially if the effectiveness of this invention is acquired.

[0049] although it may be independent or you may be any in the case of blending two or more sorts of vitamins as loadings of each vitamins -- the case of vitamin C and its salt --, 0.005 - 50 % of the weight - especially -- It is desirable to blend five to 15% of the weight, and it is desirable to blend 0.05 to 5% of the weight especially 0.0005 to 10% of the weight, when it is vitamin E, and when it is vitamin A and B-carotene, it is desirable to blend 0.5 to 5% of the weight especially 0.05 to 20% of the weight.

[0050] In this invention constituent, although the compounding ratio of a natural polyphenol extract and this invention vitamins is not limited especially as long as the purpose of this invention can be attained, it is desirable 10:1-1:10, and to carry out to especially 3:1-1:4. 10:1-1:4, prevention of as opposed to [preferably if 5:1-1:3, the operation effectiveness of a natural polyphenol extract will be heightened most, therefore] gum disease, or a curative effect will be most excellent, and especially the compounding ratio of the natural polyphenol extract in the case of combining only vitamin C with a natural polyphenol extract and vitamin C has it. [especially desirable]

[0051] In addition to a natural polyphenol extract and this invention vitamins, antibacterial vegetable extractives can be further blended with this invention constituent. Since the effectiveness which it is ineffective to it being possible to remove the stimulation to the periodontium of a gum disease original bacillus, and prevents or treats the gum disease of this invention constituent is reinforced when antibacterial vegetable extractives are blended, it is desirable.

[0052] As antibacterial vegetable extractives which can be used in this invention, an oil solubility glycyrrhiza extract, mulberry bark extractives, etc. are mentioned, for example.

[0053] Although limitation is not carried out unless the loadings of these antibacterial vegetable extractives bar the expected effectiveness of this invention especially, it is desirable to use 0.01 to 0.5% of the weight further 0.001 to 5% of the weight to the constituent whole quantity for example.

[0054] pH regulator, an organic acid, sugar-alcohol, sweetners, perfume, vitamins, bone metabolic turnover vitamins, an anti-oxidant, an excipient, a solubilizing agent, a binder, lubricant, suspension, a wetting agent, a coat morphogenetic substance, corrigent, an odor-masking agent, a coloring agent, a preservative, etc. can blend this invention constituent suitably in addition to the above-mentioned component, and it can blend suitably other additives thru/or food materials, etc. usually used for an others and physic constituent, the constituent for the oral cavities, or food formulation study. [these] About such a material, the following thing is specifically contained.

[0055] As a pH regulator, a lactic acid, pantothenic acid, phosphate, a malic acid, and a citric acid are mentioned.

[0056] Although it will not be limited to the vitamin C which is this invention vitamins and its salt, vitamin E, and a vitamin A list as vitamins especially if it is vitamins other than B-carotene, a vitamin D group, a vitamin K group, vitamin P, etc. can be blended.

[0057] As an excipient, cane sugar, a lactose, starch, grape sugar, a crystalline cellulose, mannite,

sorbitol, xylitol, erythritol, palatinit, a paratinose, maltitol, trehalose, the Lacty toll, reduction starch sugar, a reduction isomalt oligosaccharide, coupling sugar, the gum base, gum arabic, gelatin, cetyl methyl cellulose, a light silicic anhydride, ulmin acid magnesium, a meta-silicic acid calcium aluminate, a sodium hydrogencarbonate, and calcium phosphate are mentioned.

[0058] As a solubilizing agent, alcohol, ester, a polyethylene-glycol derivative, the fatty acid ester of sorbitan, and sulfated fatty alcohol are mentioned.

[0059] As a binder, a cellulosic, a carrageenan, sodium alginate, sodium polyacrylate, polylactic acid, polyglycolic acid, xanthan gum, etc. are mentioned.

[0060] Magnesium stearate, talc, hardened oil, etc. are mentioned as lubricant.

[0061] As suspension or a wetting agent, coconut oil, olive oil, sesame oil, peanut oil, a parsley oil, parsley seed oil, a calcium lactate, safflower oil, soybean phosphatide, a glycerol, a sorbitol, propylene glycol, ethylene glycol, etc. are mentioned.

[0062] As a coat morphogenetic substance, acrylic-acid system copolymers, such as carbohydrate derivatives, such as cellulose acetate phthalate, a methyl acrylate, and methacrylic acid methyl, a methacrylic acid system copolymer, etc. are mentioned, for example.

[0063] Moreover, this invention constituent may be made to contain sweeteners, such as saccharin sodium, Aspartame, stevia extractives, granulated sugar, powdered sugar, a starch syrup, salt, orange oil, water-soluble glycyrrhiza extract, menthol, and a eucalyptus oil, perfume, a coloring agent, and a preservative as corrigent or an odor-masking agent.

[0064] As a component of others which can be blended with this invention constituent, a lysine, magnesium salt, soybean isoflavone, and glycyrrhizin are mentioned.

[0065] this invention constituent can blend and prepare various well-known components which were described above according to the gestalt, and can prepare them to the various gestalten thru/or pharmaceutical form as a food constituent, the constituent for the oral cavities, and a physic constituent.

[0066] As a gestalt of a food constituent, formulation study can be carried out to the gestalt of troches, a tablet, a capsule, granulation, powdered juice, chewing gum, Kandy, a fruit gum, etc., for example.

[0067] The capsule as used in the field of this invention is a constituent which serves as a capsule coat which added plasticizers, such as a glycerol and a sorbitol, to bases, such as gelatin, from the contents of liquefied or gel by which an encapsulation is carried out to it. You may consist of a capsule coat outside hard [which makes a basis the elastic inner capsule coat which makes gelatin etc. a basis, sugar, etc. as a capsule coat]. In this invention, the grain capsule which consists of a capsule coat which consists of liquefied contents, and the above inner capsule coats and an outside capsule coat especially is desirable.

[0068] In the various gestalten of the food constituent of this invention, if a deglutition is possible for the above-mentioned active principle, i.e., a natural polyphenol extract, and this invention vitamins at least, it does not have to be good and the gum base of chewing gum etc. does not carry out a deglutition.

[0069] Moreover, the food constituent of this invention can also be used as the drink which made the dissolution or a gel bead enclose and distribute a component.

[0070] As a gestalt of the constituent for the oral cavities, dentifrices, mouth wash, the trochiscus, the pastes for the oral cavities, gel, etc. are mentioned, and a tablet, a pill, powder, liquids and solutions, suspension, an emulsion, a granule, a capsule, etc. are mentioned as a pharmaceutical form of a physic constituent, for example.

[0071] this invention constituent can be prepared [that what is necessary is just to mix a natural polyphenol extract and this invention vitamins] by the approach commonly used in the gestalt or pharmaceutical form that what is necessary is just to mix with the simultaneous or component of others separately.

[0072] as the AUW of the natural polyphenol extract (dry weight) which is usually an active principle although the intake of this invention food constituent can be suitably determined in the gestalt of food, the age of the Homo sapiens who takes in, weight, sex, health condition, etc. and it is not limited especially, and this invention vitamins -- an adult -- it is desirable to take in per kg per day and about 0.00001-1g.

[0073] as the AUW of the natural polyphenol extract (dry weight) which is usually an active principle

although the dose of this invention physic constituent can be suitably determined according to extent of the gestalt of the constituent, the age of the Homo sapiens who prescribes a medicine for the patient, weight, sex, and a disease etc. and it is not limited especially, and this invention vitamins -- an adult -- it is desirable to take in per weight per day of 1kg and about 0.00001-1g.

[0074] As a medication method of a physic constituent, there is especially no limit and it is prescribed for the patient by the approach according to extent of a pharmaceutical form, a patient's age, sex, and a disease etc. For example, in the case of a tablet which was described above, a pill, powder, liquids and solutions, suspension, an emulsion, a granule, and a capsule, it is administered orally.

[0075] By using a natural origin polyphenol extract for vitamin C (and the salt), vitamin E, and a vitamin A list combining one or more sorts of B-carotene, the inhibition effectiveness of MMPs is reinforced and this invention constituent prepared as mentioned above has the outstanding gum disease preventive effect. Moreover, since the polyphenol extract of the natural product origin with few side effects by recipe and intake is used for this invention constituent as compared with the MMPs inhibitor of a synthetic system, its safety is high and prolonged use is possible for it.

[0076] Although this invention constituent has the operation which controls production of the periodontium cell origin MMPs and it has the operation which checks growth control of a periodontium cell, these operations when nicotine has received the stimulus are more excellent compared with the case where a stimulus of nicotine is not received. Therefore, when an smoker thru/or a passive smoker take in or use this invention constituent, it is possible to prevent or treat gum disease more effectively.

[0077] Thus, this invention constituent which has the outstanding gum disease prevention thru/or the outstanding curative effect has high safety, and can be used as the gum disease prevention which can be used for a long period of time, or a therapy constituent.

[0078] Moreover, when using this invention constituent as a food constituent, it is also possible to be able to expect prevention or the curative effect of gum disease, and to take in as health food and a food for specified health use.

[0079] Also when using this invention constituent as a constituent for the oral cavities, the outstanding gum disease prevention or the outstanding curative effect can be expected, and it can be used also as quasi drugs.

[0080] Moreover, it is also expectable by taking in or using this invention food constituent or the constituent for the oral cavities during the therapy of gum disease that a curative effect improves.

[0081] this invention food or the constituent for the oral cavities is (A) especially, although it can be used for prevention or the therapy of gum disease. It is (B) to one sort or two sorts or more, and list which are chosen from the extract containing natural polyphenol. It is desirable to use it as the food constituent for gum disease prevention containing one sort chosen from the group which becomes vitamin C and its salt, vitamin E, and a vitamin A list from B-carotene, or two sorts or more, or a constituent for the oral cavities for gum disease prevention.

[0082] Since the inhibition effectiveness of MMPs is reinforced and the polyphenol extract of the natural product origin with few side effects by recipe and intake is used as compared with the MMPs inhibitor of a synthetic system, a natural polyphenol extract and the constituent containing one or more sorts of vitamin C (and the salt), vitamin E, vitamin A, and B-carotene are expensive, and as described above, since prolonged use is possible, safety can use them also as MMPs inhibitor. Therefore, the constituent which contains one sort of B-carotene (this invention vitamins) or two sorts or more at vitamin C and its salt, vitamin E, and a vitamin A list in one sort of a natural polyphenol extract or two sorts or more, and a list can be used as MMPs inhibitor.

[0083] the extract list containing the natural polyphenol in the MMPs inhibitor concerned -- the class of vitamins, such as vitamin C, thru/or loadings; -- the class of other components, such as antibacterial vegetable extractives, thru/or loadings; -- the gestalt of MMPs inhibitor thru/or pharmaceutical form; -- suppose that it is the same as that of this invention food constituent, a constituent for the oral cavities, or a physic constituent which was described above about the preparation approach of MMPs inhibitor, intake or a dose, and a medication method.

[0084] Therefore, the above-mentioned MMPs inhibitor can be used as a food constituent, the

constituent for the oral cavities, or a physic constituent.

[0085] moreover, as natural polyphenol contained in the natural polyphenol extract blended with the above-mentioned MMPs inhibitor Rheumatoid arthritis, the periosteum in the osteoarthritis, and articular cartilage organization; cornea tissue; periodontium; The natural polyphenol which has inhibition activity to the cell origins MMPs, such as a cancer organization, in a list is desirable. Since what has inhibition activity especially to the periodontium cell origin MMPs is desirable, especially the above-mentioned MMPs inhibitor can expect that the inhibition activity excellent in these cell origin MMPs will be shown.

[0086]

[Example] Although the example of a trial, an example, and the example of a comparison explain this invention still more concretely below, this invention is not restricted to the following example of a trial and a following example.

[0087] The inhibition effectiveness by the extract which contains the natural polyphenol of a publication in the following "following 1 and ingredient" over the living body origin MMP (collagenase, gelatinase) which participates in destruction of example of trial 1 periodontium was examined.

[0088] 1 Ingredient 1-1, Subject natural extract grape seed extractives tea extract blueberry EKISU Silymarin extractives.

[0089] 1-2, Positive control tetracycline.

[0090] 1-3 Two kinds of following collagenases were used as collagenase collagenase.

[0091] What refined the Homo sapiens pro collagenase made to produce in the Dulbecco strange method MEM culture medium of a non-blood serum, using an HGF cell as collagenase of the Homo sapiens gum fibroblast (it abbreviates to "HGF cell" henceforth) origin using CM sepharose TM (Pharmacia manufacture) and zinc KIRETINGU sepharose TM (Pharmacia manufacture), and was activated after dissolving in the buffer solution was used. Activation was performed by incubating at 37 degrees C for 4 hours, using aminophenyl mercury acetate (sigma company make) as an activator.

[0092] Moreover, what refined the Homo sapiens pro collagenase made to produce in the culture medium for epithelia of a non-blood serum, using a HGK cell as collagenase of the Homo sapiens gingival-epithelium cell (it abbreviates to "HGK cell" henceforth) origin using CM sepharose TM (Pharmacia manufacture) and zinc KIRETINGU sepharose TM (Pharmacia manufacture), and was activated like the above after dissolving in the buffer solution was used.

[0093] 1-4 As gelatinase gelatinase, the gelatinase of the HGF cell origin and the gelatinase of the HGK cell origin were used.

[0094] It is gelatin sepharose respectively about the Homo sapiens pro gelatinase which made the Homo sapiens pro gelatinase made to produce in the Dulbecco strange method MEM culture medium of a non-blood serum, using an HGF cell as gelatinase of the HGF cell origin produce by the culture medium for epithelia, using a HGK cell as gelatinase of the HGK cell origin. What was activated by the same approach as collagenase was used after purification using 4BTM (Pharmacia manufacture).

[0095] 2-1 Measurement of the inhibition effectiveness of the extract containing the natural polyphenol of the above 1-1 to the measurement collagenase of the inhibition effectiveness to collagenase was performed with fluorescein isothiocyanate by measuring collagenase activity according to the approach (referring to Japanese Journal of Inflammation, four volumes, 123 pages, and 1984) of Nagai and others who made the substrate the I-beam collagen (product made from YAGAI) by which the indicator was carried out. That is, the activated Homo sapiens collagenase (2U/ml) of 40microl, and the substrate of 50microg and the examined substance which dissolved in the assay buffer of 40microl were mixed, and it was made to react at 37 degrees C for 4 hours. Collagenase activity of control (examined substance un-adding) was made into 100%, and IC50 value which shows a trial dose required to prevent 50% from the reduction degree of the collagenase activity at the time of various examined substance addition was calculated. Moreover, the tetracycline it is reported that the inhibition effectiveness over collagenase activity is was made into positive control, and the comparison with a subject natural extract was performed.

[0096] 2-2 Measurement of the inhibition effectiveness of the extract containing the natural polyphenol

of the above 1-1 to the measurement gelatinase of the inhibition effectiveness to gelatinase made the substrate IV mold collagen (product made from YAGAI) by which the indicator was carried out with fluorescein isothiocyanate, and was performed by the same approach as measurement (2-1) of the inhibition activity over the above-mentioned collagenase. However, reaction temperature was made into 42 degrees C. It measured by the approach with the same said of a tetracycline.

[0097] The measurement result of the enzyme inhibition activity over HGF cell origin collagenase and gelatinase is shown in Table 1 at HGK cell origin collagenase and gelatinase, and a list.

[0098]

[Table 1]

		表 1				
		50%阻害濃度(μg/ml)				
試料	コラゲナーゼ		ゼラチナーゼ		阻害効果	
	HGF	HGK	HGF	HGK		
本発明で用い る、天然ポリ フェノールを 含む抽出物	ブドウ種子エキス	1. 2	2. 3	1. 0	1. 9	+++
	茶抽出物	5. 4	6. 6	7. 8	8. 1	++
	ブルーベリーエキス	9. 4	11. 2	6. 5	7. 3	++
	シリマリンエキス	76. 0	82. 4	55. 0	62. 4	+
比較化合物	テトラサイクリン	2. 5	3. 2	8. 7	9. 2	+++

H G F : ヒト歯肉線維芽細胞

H G K : ヒト歯肉上皮細胞

+++ : 非常に効果あり

++ : 効果あり

+

- : 効果なし

[0099] The MMP inhibition effectiveness was checked by the grape seed extractives used as an extract containing natural polyphenol, a tea extract, blueberry extractives, and the Silymarin extractives in this invention. As compared with the tetracycline by which especially grape seed extractives are known as a collagenase inhibitor, an EQC or the MMP inhibition activity beyond it was checked.

[0100] In the following examples 2-4 of a trial, what was used combining grape seed extractives, a tea extract, blueberry extractives or the Silymarin extractives, and vitamin C or vitamin E was made into the example 1 - the example 4, respectively.

[0101] Moreover, that for which only vitamin C used only vitamin E was made into the example 1 of a comparison thru/or the example 2 of a comparison. What used grape seed extractives or a tea extract combining coenzyme Q 10, respectively was made into the example 3 of a comparison thru/or the example 4 of a comparison.

[0102] The inhibition effectiveness over collagenase production of example of trial 2 Homo-sapiens gum fibroblast and a Homo sapiens gingival-epithelium cell was examined.

[0103] About 1 and an ingredient, the same thing as the example 1 of a trial was used in the examples 3 and 4 of a comparison except having used coenzyme Q 10, using vitamin C and vitamin E as a subject vitamin.

[0104] The amount of grape seed extractives, tea extract, blueberry extractives, and Silymarin extractives ** used was 100microg/ml. Moreover, the amount of the example 1 of a comparison, the vitamin C in 2, or the vitamin E used was 50microg/ml.

[0105] 10,000 piece / well seeding of an HGF cell and the HGK cell were carried out to the plate for tissue culture of measurement 96 hole of the inhibition effectiveness over 2 and collagenase production of a cell, respectively, the HGK cell was diluted with 37 degrees C at the Dulbecco strange method MEM culture medium (DMEM) which will contain an examined substance and 1% fetal calf serum for an HGF cell after incubation for one day, respectively to the culture medium for epithelia containing an examined substance and 1% fetal calf serum, and it incubated for two days by the obtained culture medium. Furthermore, it changed to DMEM or the culture medium for non-blood serum epithelia which does not contain an examined substance for a culture medium and which contains only fetal calf serum 1%, and incubated for two days, and the amount of the collagenase which separates in a culture medium

was measured using the approach of Nagai and others who indicated by 2-1 of the example 1 of a trial. Moreover, collagenase activity of the culture-medium supernatant liquid of control (examined substance un-adding) was made into 100%, and it asked for the relative rate of the collagenase activity at the time of various examined substance addition. The measurement result of the inhibition activity over MMP production of an HGF cell and a HGK cell is shown in Table 2.

[0106]

[Table 2]

表 2

	被験物質		コラゲナーゼ産生の阻害率(%)	
	試料	同時添加物 (50 μ g/ml)	(併用時阻害率増加割合(%))	
			HGF	HGK
実施例	1 ブドウ種子エキス	なし	30	36
		ビタミンC	62 (32)	58 (22)
		ビタミンE	48 (18)	52 (16)
	2 茶抽出物	なし	25	28
		ビタミンC	44 (19)	39 (11)
		ビタミンE	47 (22)	49 (21)
	3 ブルーベリーエキス	なし	21	18
		ビタミンC	41 (20)	36 (18)
		ビタミンE	32 (11)	25 (7)
	4 シリマリンエキス	なし	14	11
		ビタミンC	32 (18)	35 (24)
		ビタミンE	21 (7)	24 (13)
比較例	1 ビタミンC	なし	—	—
	2 ビタミンE	なし	—	—
	3 ブドウ種子エキス	補酵素Q10	32 (2)	39 (3)
	4 茶抽出物	補酵素Q10	28 (3)	29 (1)

- ・表中、HGFはヒト歯肉線維芽細胞を表し、HGKはヒト歯肉上皮細胞を表す。
- ・天然ポリフェノールを含む抽出物（天然ポリフェノール抽出物）と他の成分を併用した場合の阻害率から、天然ポリフェノール抽出物の単独使用時の阻害率を引いたものを、併用時阻害率増加割合(%)とした。尚、各実施例において、天然ポリフェノール抽出物の単独使用時の阻害率を併記しておく（〔同時添加物：なし〕に相当する）。
- ・表中、比較例1及び比較例2の「—」は、「阻害効果なし」を意味する。

[0107] Raising the inhibition activity over MMP production of a cell effectively according to concomitant use with a natural polyphenol extract, and vitamin C or vitamin E was checked.

[0108] Although it is well-known to use together grape seed extractives and coenzyme Q 10, as shown in the example 3 of a comparison, the increment percentage of the rate of inhibition by the concomitant use concerned is several %. On the other hand, as shown in an example 1, the grape seed extractives of this invention, vitamin C, or the increment percentage by concomitant use with vitamin E is dozens of %, and it turns out that the combined effect by the combination of this invention is excellent. In addition, when a tea extract, vitamin C, or vitamin E was combined, the same effectiveness was shown as compared with concomitant use with coenzyme Q 10 and a tea extract (example 2 and example of

comparison 4 reference).

[0109] As described above example of trial 3, it is reported by the in vitro trial that the nicotine which is the main stimulator in cigarette smoke does bad influences, such as growth control of a cell and increase of collagenase production, to a periodontium cell. Then, the production inhibition effectiveness by concomitant use with the natural polyphenol extract to collagenase production of the Homo sapiens gum fibroblast which increased by stimulus of nicotine, and a Homo sapiens gingival-epithelium cell, and vitamin C or vitamin E was examined.

[0110] 1, About the ingredient, others used the same thing as the example 1 of a trial, using vitamin C or vitamin E as a subject vitamin.

[0111] 2, It measured like the approach indicated in the example 2 of a measurement trial of the inhibition effectiveness over the collagenase production of a cell which performed the nicotine stimulus. However, nicotine was added 0.05% with an examined substance and 1% fetal calf serum to the culture medium. Collagenase activity of the culture-medium supernatant liquid of control (only nicotine addition culture medium) was made into 100%, and it asked for the relative rate of the collagenase activity at the time of various examined substance addition. A result is shown in Table 3.

[0112]

[Table 3]

表 3

	被 験 物 質		ニコチン刺激コラゲナーゼ 産生の阻害率(%) (併用時阻害率増加割合(%))	
	試料	同時添加物 (50 μ g/ml)		
			HGF	HGK
実 施 例	1 ブドウ種子エキス	なし	15	21
		ビタミンC	55 (40)	48 (27)
		ビタミンE	42 (27)	32 (11)
	2 茶抽出物	なし	11	13
		ビタミンC	48 (37)	39 (26)
		ビタミンE	45 (34)	43 (30)
	3 ブルーベリーエキス	なし	8	12
		ビタミンC	37 (29)	41 (29)
		ビタミンE	41 (33)	40 (28)
	4 シリマリンエキス	なし	5	7
		ビタミンC	37 (32)	35 (28)
		ビタミンE	35 (30)	32 (25)
比 較 例	1 ビタミンC	なし	—	—
	2 ビタミンE	なし	—	—

- ・表中、HGFはヒト歯肉線維芽細胞を表し、HGKはヒト歯肉上皮細胞を表す。
- ・天然ポリフェノール抽出物と他の成分を併用した場合の阻害率から、天然ポリフェノール抽出物の単独使用時の阻害率を引いたものを、併用時阻害率増加割合(%)とした。尚、各実施例において、天然ポリフェノール抽出物の単独使用時の阻害率を併記しておく（「同時添加物：なし」に相当する）。
- ・表中、比較例1及び比較例2の「—」は、「阻害効果なし」を意味する。

[0113] by addition of nicotine, the increment in the collagenase production from a subject cell shows -- having (increase of nicotine additive-free 380%) -- by using together the natural polyphenol extract used by this invention, vitamin C, or vitamin E shows that the outstanding inhibition activity is shown to the collagenase production which increased by stimulus of nicotine.

[0114] Moreover, as compared with the result of the example 2 (Table 2) of a trial which does not add nicotine, raising the inhibition activity over collagenase production further according to concomitant use was checked in the cell which performed the nicotine stimulus.

[0115] The effect by concomitant use of a natural extract, vitamin C, etc. which were indicated for the above-mentioned example 1 of a trial over the cell proliferation activity controlled by stimulus of nicotine by the example of trial 4 pan was considered.

[0116] 1, About the ingredient, others used the same thing as the example 1 of a trial, using vitamin C or vitamin E as a subject vitamin.

[0117] 2, On the plate for tissue culture of measurement 96 hole of the effect to the cell proliferation which performed the nicotine stimulus, 5,000 piece / well inoculation of an HGF cell and the HGK cell were carried out, respectively, and it incubated at 37 degrees C on the 1st. Then, these cells were diluted,

respectively to the Dulbecco strange method MEM culture medium (HGF cell) or the culture medium for epithelia (HGK cell) containing an examined substance, 0.05% nicotine, and 1% fetal calf serum, it incubated for five days by the obtained culture medium, and those cell proliferation activity was measured. Moreover, the culture medium which added only nicotine was used for the culture medium as contrast. The cell was fixed with the formalin solution 10% after culture for five days about each examined substance, it dyed by the crystal violet, and the number of cells was measured from the absorbance in 590nm. It asked for the relative rate of the various examined substances at the time of making into 100% the enumerated data of contrast (culture medium which added only nicotine). The measurement result of the effect to the cell proliferation activity from the HGF cell which received the nicotine stimulus, and a HGK cell is shown in Table 4.

[0118]

[Table 4]

表 4

	被験物質		ニコチン刺激細胞増殖率(%)	
	試料	同時添加物 (50 μ g/ml)	(併用時増殖率増加割合(%))	
			HGF	HGK
対照	ニコチン単独添加培地	なし	100	100
実施例	1 ブドウ種子エキス	なし	125	131
		ビタミンC	165 (40)	149 (18)
		ビタミンE	159 (34)	152 (21)
	2 茶抽出物	なし	115	124
		ビタミンC	131 (16)	147 (23)
		ビタミンE	142 (27)	157 (33)
	3 ブルーベリーエキス	なし	109	113
		ビタミンC	124 (15)	131 (18)
		ビタミンE	135 (26)	146 (33)
	4 シリマリンエキス	なし	113	109
		ビタミンC	146 (33)	133 (24)
		ビタミンE	122 (9)	125 (16)
比較例	1 ビタミンC	なし	—	—
	2 ビタミンE	なし	—	—

- ・表中、HGFはヒト歯肉線維芽細胞を表し、HGKはヒト歯肉上皮細胞を表す。
- ・天然ポリフェノール抽出物と他の成分を併用した場合の増殖率から、天然ポリフェノール抽出物の単独使用時の増殖率を引いたものを、併用時増殖率増加割合(%)とした。尚、各実施例において、天然ポリフェノール抽出物の単独使用時の増殖率を併記しておく(「同時添加物：なし」に相当する)。
- ・表中、比較例1及び比較例2の「—」は、「対照と比較して変化なし」を意味する。

[0119] by adding in a culture medium, control of cell proliferation shows nicotine -- having (a nicotine additive-free 52% decrease) -- in simultaneous adding with the natural polyphenol extract of this invention, vitamin C, or vitamin E, it was checked that the inhibition activity over the cell proliferation

depressant action of nicotine is raised.

[0120] Below, the example of a formula of this invention constituent is indicated. As long as there is especially no publication, these constituents are prepared according to a conventional method.

[0121] Example 5 The chewing gum which blended chewing gum grape seed extractives, vitamin E, the tea extract, and the oil solubility glycyrrhiza extract was prepared by the next formula.

[0122]

A calcium carbonate 5.00 grape seed extractives 2.00 vitamin E A 0.01 tea extract A 1.00 oil-solubility glycyrrhiza extract The 0.05 gum base 27.00 erythritol 10.00 xylitol 38.00 maltitol 12.00 perfume Remainder meter The 100.00 weight sections.

[0123] Example 6 The solution 60 weight section in a capsule was entirely wrapped in the inner capsule coat 40 weight section which consists of grain capsule gelatin and a sorbitol, and the grain capsule was prepared by carrying out glycocalyx in the outside capsule coat 110 weight section which consists of sugar further.

[0124]

カプセル内溶液

ビタミンC	7.2
ビタミンE	2.4
ブドウ種子エキス	12.0
茶抽出物	12.0
グリセリン脂肪酸エステル	1.0
紅花油	残部
計	60重量部。

[0125]

内カプセル皮膜

ゼラチン	36.0
ソルビトール	残部
計	40.0重量部。

[0126]

外カプセル皮膜

油溶性甘草エキス	0.3
卵殻カルシウム	1.0
アスパルテーム	0.1
アラビアガム	0.6
ゼラチン	0.2
香料	0.4
カルバナワックス	0.1
シェラック	0.3
パラチニット	残部
計	110.0重量部。

[0127] Example 7 The tablet which blended tablet vitamin C, vitamin E, grape seed extractives, the tea extract, and the oil solubility glycyrrhiza extract was prepared by the next formula.

[0128]

ビタミンC	9.0
粉末ビタミンE	1.0
(d- α -トコフェロール20%含有)	
ブドウ種子エキス	12.0
茶抽出物	12.0
油溶性甘草エキス	1.0
ポリデキストロース	7.0
シュガーエステル	2.0
香料	1.0
キシリトール	15.0
パラチノース	40.0
計	100.0重量部。

[0129] Example 8 The mouth deodorant which carried out the glycolyx of the tablet partial 200 weight section which blended glycolyx tablet vitamin C, vitamin E, vitamin A, grape seed extractives, and a tea extract in the glycolyx section 130 weight section which blended the oil solubility glycyrrhiza extract was created.

[0130]

錠剤部分

ビタミンC	5.00
ビタミンE	1.50
ビタミンA	0.50
ブドウ種子エキス	8.50
茶抽出物	8.50
シュガーエステル	1.00
グアーガム	0.20
アスパルテーム	0.01
香料	1.00
パラチノース	残部
計	100.00重量部。

[0131]

糖衣部

油溶性甘草エキス	0.12
リン酸3カルシウム	1.00
アスパルテーム	0.01
アラビアガム	0.50
香料	0.40
カルバナワックス	0.10
シェラック	0.20
マルチトール	残部
計	100.00重量部。

[0132] Example 9 Kandy which blended Kandy grape seed extractives, a tea extract, vitamin C, and mulberry bark extractives was created by the next formula.

[0133]

ブドウ種子エキス	1.0
茶抽出物	1.0
ビタミンC	5.0
桑白皮エキス	0.1
キシリトール	8.0
マルチトール	10.0
アスパルテーム	0.1
香料	0.2
バラチニット	残部
計	100.0重量部。

[0134] Example 10 The gel which melted the bead in drink **** following formula to homogeneity was dropped into 5% calcium-lactate solution, and the spherical vitamin bead was obtained.

[0135]

ビタミンビーズ処方

ビタミンE	0.10
(d- α -トコフェロール67%含有)	
油溶性甘草エキス	0.02
エリスリトール	15.00
ステビア	0.05
アルギン酸ナトリウム	1.00
色素	0.05
脱イオン水	残部
計	100.00重量部。

[0136] The above-mentioned vitamin bead was blended with the drink of the following formula.

ブドウ種子エキス	0.05
ビタミンC	1
1%ジェランガム	10
エリスリトール	15
ステビア	0.1
香料	0.2
ビタミンビーズ	7
50%クエン酸溶液	pH 3.7 に調整
脱イオン水	残部
計	100.00重量部。

[0137]

Example 11 ***** Dibasic calcium phosphate 30.00 Glycerol 10.00 Sorbitol 20.00 Carboxymethylcellulose sodium 1.00 Sodium lauryl sulfate 1.50 Carrageenan 0.50 Saccharin sodium 0.10 perfume 1.00 Sodium benzoate 0.30 grape seed extractives 0.05 Vitamin E 0.05 Oil solubility glycyrrhiza extract 0.05 Water Remainder Total The 100.00 weight sections.

[0138]

実施例 1 2 洗口液

エタノール	10.00
グリセリン	5.00
クエン酸	0.01
クエン酸ナトリウム	0.10
ポリオキシエチレン硬化ひまし油	0.50
パラオキシ安息香酸メチル	0.10
香料	0.20
ブドウ種子エキス	0.05
ビタミンE	0.05
ビタミンC	0.01
水	残部
計	100.00重量部。

[0139]

実施例 1 3 トローチ

マルチトール	21.00
アラビアガム	1.50
ショ糖脂肪酸エステル	2.50
粉末香料	1.00
クエン酸	4.00
ブドウ種子エキス	0.10
ビタミンC	10.00
油溶性甘草エキス	0.05
キシリトール	残部
計	100.00重量部。

[0140]

Example 14 Paste for the oral cavities Liquid paraffin 13 Cetanol 10 Glycerol 25 Sorbitan monopalmitate 0.6 Polyoxyethylenesorbitan monostearate 5 Sodium lauryl sulfate 0.1 Chlorination benzoTONIUMU 0.1 Methyl salicylate 0.1 Saccharin 0.2 Perfume 0.25 Grape seed extractives 0.10 Vitamin E 0.05 Oil solubility glycyrrhiza extract 0.05 Water Remainder Total The 100.00 weight sections.

[0141]

実施例 1 5 口腔用ゲル

カルボキシメチルセルロース	0.2
グリセリン	40
ブドウ種子エキス	1
ビタミンE	0.05
水	残量
全量	100(重量%)。

[0142] Example 16 The solution 60 weight section in a capsule was entirely wrapped in the inner capsule coat 40 weight section which consists of grain capsule gelatin and a sorbitol, and the grain capsule was prepared by carrying out glycocalyx in the outside capsule coat 110 weight section which consists of sugar further.

[0143]

カプセル内溶液

ビタミンC	25.0
ブドウ種子エキス	10.0
茶抽出物	10.0
グリセリン脂肪酸エステル	1.0
紅花油	残部
計	60重量部。

ゼラチン	36.0
ソルビトール	残部
計	40.0重量部。

[0144] Inner capsule coat

[0145]

外カプセル皮膜

油溶性甘草エキス	0.3
卵殻カルシウム	1.0
アスパルテーム	0.1
アラビアガム	0.6
ゼラチン	0.2
香料	0.4
カルバナワックス	0.1
シェラック	0.3
パラチニット	残部
計	110.0。

[0146] The above-mentioned example shows the concrete mode of this invention, and this invention is not limited to the above-mentioned example. Moreover, the following modes are also contained in this invention.

[0147] Term I (A) One sort or two sorts or more which are chosen from the extract containing the natural polyphenol which has periodontium cell origin matrix METARO protease inhibition activity, One sort or two sorts or more which are chosen as a list from the group which becomes from B-carotene at (B) vitamin C and its salt, vitamin E, and a vitamin A list, The gum disease prevention to contain or the constituent for the oral cavities for a therapy, term I-1 A constituent given in the term I which is a constituent for the oral cavities for gum disease prevention, Term I-2 (A) The extract containing natural polyphenol Grape seed extractives, The term I which is one sort chosen from the group which consists of a tea extract, blueberry extractives, and Silymarin extractives, or two sorts or more, or a constituent given in I-1, Term I-3 It is (C) further. A constituent given in either of term I-I -2 containing antibacterial vegetable extractives, Term I-4 (C) A constituent given in the term I-3 which is one sort chosen from the group which antibacterial vegetable extractives become from an oil solubility glycyrrhiza extract and mulberry bark extractives, or two sorts, Term I-5 Constituent given in either of term I-I -4 especially useful to an smoker which has the depressant action of the periodontium cell origin matrix METARO protease production by nicotine stimulus.

[0148] Term II (A) One sort or two sorts or more which are chosen from the extract containing the natural polyphenol which has periodontium cell origin matrix METARO protease inhibition activity, One sort or two sorts or more which are chosen as a list from the group which becomes from B-carotene at (B) vitamin C and its salt, vitamin E, and a vitamin A list, The gum disease prevention to contain or the physic constituent for a therapy, term II-1 (A) The extract containing natural polyphenol A constituent given in the term II which is one sort chosen from the group which consists of grape seed

extractives, a tea extract, blueberry extractives, and Silymarin extractives, or two sorts or more, term II-2 -- further -- (C) the term II containing antibacterial vegetable extractives, or a constituent given in II-1 -- Term II-3 (C) A constituent given in term II-2 which are one sort chosen from the group which antibacterial vegetable extractives become from an oil solubility glycyrrhiza extract and mulberry bark extractives, or two sorts, Term II-4 Constituent given in either of term II-II -3 especially useful to an smoker which has the depressant action of the periodontium cell origin matrix METARO protease production by nicotine stimulus.

[0149]

[Effect of the Invention] The constituent of this invention has the operation of the outstanding gum disease prevention or a therapy. Moreover, since the extract with which the side effect by recipe and intake contains little natural polyphenol is used in this invention constituent as compared with the MMPs inhibitor of a synthetic system, safety is high, prolonged use is possible, and it is useful as the food constituent, the constituent for the oral cavities, or physic constituent for gum disease prevention or a therapy.

[0150] Furthermore, this invention constituent can prevent or treat gum disease more effectively, when an smoker thru/or a passive smoker took in or use it.

[Translation done.]